Annual Report

Year 1981

The Division of Research Services

The many specialized functions of the Division are designed to support all of the 18 Bureaus, Institutes, and Divisions (BIDs) which constitute the National Institutes of Health. The primary program emphasis, however, is directed at serving the 8,000 staff members of the intramural program, including more than 2,600 doctoral level scientists who conduct research in NIH laboratories.

Organizationally, the Division is structured to provide products and services in support of the sequential steps in every biomedical research project: planning, making available models and substrates, manipulating and measuring research materials, and recording and communicating research results.

- The Library Branch possesses or has access to virtually all published biomedical knowledge to assist the investigator in planning and designing his/her project.
- The Veterinary Resources Branch provides the animal models, organic materials, and proper facilities for their use.
- The Biomedical Engineering and Instrumentation Branch collaborates with the investigator in devising the means whereby research materials may be manipulated and results measured, often with highly sophisticated electronic equipment.
- Finally, the skills of the Medical Arts and Photography Branch are available to all investigators to enable them to record and communicate the results of their research to the scientific community.

A Letter From the Director

Joe R. Held, D.V.M., Director
Director of Research Services
National Institutes of Health

Throughout this report one will find repeated references to the various measures the Division's four Branches are taking to make their operations more efficient—to save money—yet maintain the high quality of their services to NIH biomedical investigators. It is worth noting something about the process by which these efficiencies are being achieved and how more can be realized in the future.

In responding effectively to the changing needs and priorities of NIH research programs, we have learned the key to providing services efficiently is to have a staff with the skills and talents to collaborate directly in projects being conducted by biomedical scientists. Our people become part of the research team. They are there at the beginning, the middle, and the end.

This allows us to determine precisely what services will be required for a project and when they will be needed. With this information we are able to plan and organize the most cost-effective way of delivering the services, either by having our own people do the work or contracting it out to industry.

An example of one way the process works to the benefit of NIH research can be found in the development this year of new imaging devices by the Biomedical Engineering and Instrumentation Branch (BEIB). One of the systems, a positron emission tomographic scanner (NEURO-PET), was conceived by scientists at the National Institute of Neurological and Communicative Diseases and Stroke. BEIB designed the mechanical and electronic parts of the system while the fabrication of a novel ring of scintillation crystals and the high speed electronic circuits was performed by private industry under contract. With the scientists, BEIB engineers, and industry working together, the system is being built to the desired specifications. Costs are being reduced by BEIB handling the design and management of the project.

As the level of our staff's expertise has risen, the degree of collaboration has increased. Some indicators of this trend:

- BEIB has a physical sciences group located at the Clinical Center working with the various Institutes on the solution of biomedical problems in patients. These joint investigations range from the development of immuno-fluorescent tagging and cell counting techniques showing the responses of cancer cells to chemotherapy to learning the role hormones play in regulating body temperature, a new field of study. Members of the BEIB group supply the engineering expertise in developing devices that are integral to the experiments, such as various types of flow cytometers.
- To meet the needs of scientists for new immunological studies, a geneticist in the Veterinary Resources Branch has bred a strain of mouse which is both B-cell and T-cell deficient, making it virtually lacking in immune response and therefore an important tool in the understanding of immune processes and their role in autoimmune diseases, as well as various infectious diseases. Collaboration also is underway with cancer investigators to extend immunology research further by breeding a strain of mouse which also is genetically lacking in a system known as "natural killer cells" (NK), thought to be involved in regulating the growth of metastases.
- Our Library specialists perform another kind of collaborative role—making sure investigators have access to all of the scientific information they need for their work, culling it from more than 150 data bases of medical literature. This year, these specialists performed more than 35,000 literature searches by subject, author, experimental technique, and animal type. The searches included monthly updates during the course of projects and final updates requested by investigators as they were about to publish the results of their work.
- Publication is a collaborative process, too. Artists and photographers in the Medical Arts and Photography Branch work directly with scientists in devising innovative ways to illustrate their work. This year, new techniques were being developed to allow multiple camera filming of extended surgical and scientific procedures while they are in progress.

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Another indication of how the Division is performing may be seen in the more than 50 scientific papers authored or co-authored by DRS staff during FY 1981, many of them in collaboration with investigators in other Institutes. The output of scientific papers also reflects the changing character of the Division's staff, which now has a considerably higher ratio of doctoral level personnel than a few years ago.

Planning Future Economies

Instilling efficiencies in the Division's operations takes many forms. A principle that has been adhered to for several years is to contract out services that can be supplied at lower cost—at no sacrifice in quality—by private industry. This has been applied increasingly to the procurement of laboratory animals, obtainable from suppliers who specialize in the mass production of certain strains.

Some of the savings from contract procurement unavoidably are offset by the necessity for the Division to maintain staff able to screen and assure that purchased animals and services meet rigid NIH standards of quality. This control prevents scientific work at the Institutes from being compromised, which is another type of cost saving.

The Division constantly seeks to expand the use of automation where savings can be demonstrated; to modernize facilities and reduce operating costs; and to install central services for use by all NIH intramural programs, rather than provide duplicate services for individual Institutes. These applications have been born out of recognition that resources are finite, that we have to make our whole operation more cost-effective as well as assist the entire intramural program in becoming more efficient. Here are some ways we see significant cost savings being achieved over the near and long terms:

- **Cryopreservation** - Management of VRB-produced laboratory animals which model human diseases will be enhanced by use of a sperm and embryo bank. Valuable strains will be safeguarded against possible catastrophic loss through disease at a lower cost. Long range savings are expected in maintaining up to 60 percent of stocks and strains in the Genetic Resource through cryopreservation of embryos.
- **Improved facilities** - For the first time, the Division will offer central research rodent holding services in FY 1982 to promote efficiency. This is being accomplished through renovation of Building 14B. Facilities at the NIH Animal Center will be upgraded to produce dogs more efficiently, upgrade the health quality of goats, and protect expensive farm machinery.
- **Primate supplies** - Assistance is being given to an international primate supply program being developed by the World Health Organization to assure the availability of species for human health research. This is being done through cost-effective breeding and conservation programs.
- **Inventory automation** - Implementation is planned for a comprehensive computer system for the more efficient maintenance of animal inventories, billing procedures, and management of rodent colonies in the Genetic Resource.
- **Library automation** - An automated system to be installed in FY 1982 will provide a data base showing the complete holdings of the NIH Library and allow label machine reading for the collection. An automated circulation control system is planned for FY 1983. A more efficient microfiche printing system to produce photocopies also is scheduled for introduction in FY 1982.
- **Graphic automation** - The Medical Arts and Photography Branch is installing a computer graphics system to shorten production times and reduce costs for rendering charts, graphs, and other displays explaining the work of scientific investigators.
- **Central microanalytic facility** - The existing electron microprobe and electron energy loss spectrometer capabilities are being extended in response to the needs of NIH investigators. In addition, a novel mass spectrometric facility is being assembled to explore more efficient ion sources (secondary ionization mass spectrometry), which should permit the measurement of molecular weights and structural subgroups of minute amounts of biologically important molecules. Development of an NMR imaging system has reached a stage where it can be applied to animal and human subjects for the diagnosis of such pathological conditions as hydrocephalus in neonates. Common use of this equipment by investigators will achieve efficiencies in operating costs while advancing biomedical knowledge.
- **Rental program** - BEIB's scientific equipment rental program is continuing to expand, enabling investigators throughout NIH to effect significant cost savings. Currently there are more than 1,800 pieces of equipment valued at $4.4 million in the inventory.

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Financial Operations

During FY 1981, cost-effective measures enabled the Division to increase its output of services over the previous year with only a 6.5 percent increase in the budget, which did not offset the inflation factor. The budget, originally targeted at $28.7 million, was reduced by nearly $500,000 in the middle of the year. This left an increase of $1,730,000.

The largest portion of the increase—$1 million—was applied to the contracting for design graphic services formerly paid for directly by the Institutes. The remaining $730,000, or 2.8 percent of the increase, was applied principally toward an authorized 9 percent pay increase and inflation in other costs.

In the coming year, the Division intends to continue its tight rein on expenses while providing more of the same high quality services to the NIH intramural program. We are confident of our staff's ability to meet the challenges that lie ahead.

Division of Research Services
Annual Budget
(In thousands of dollars)

	FY-80	FY-81	Increase/ Decrease
Veterinary Resources	$11,228	$11,561	+ $333
Biomedical Engineering & Instrumentation	$ 8,114	$ 8,339	+ $225
Library	$ 2,509	$ 2,561	+ $ 52
Medical Arts & Photography	$ 4,598	$ 5,718	+ $1,120
Total	$26,449	$28,179	$1,730

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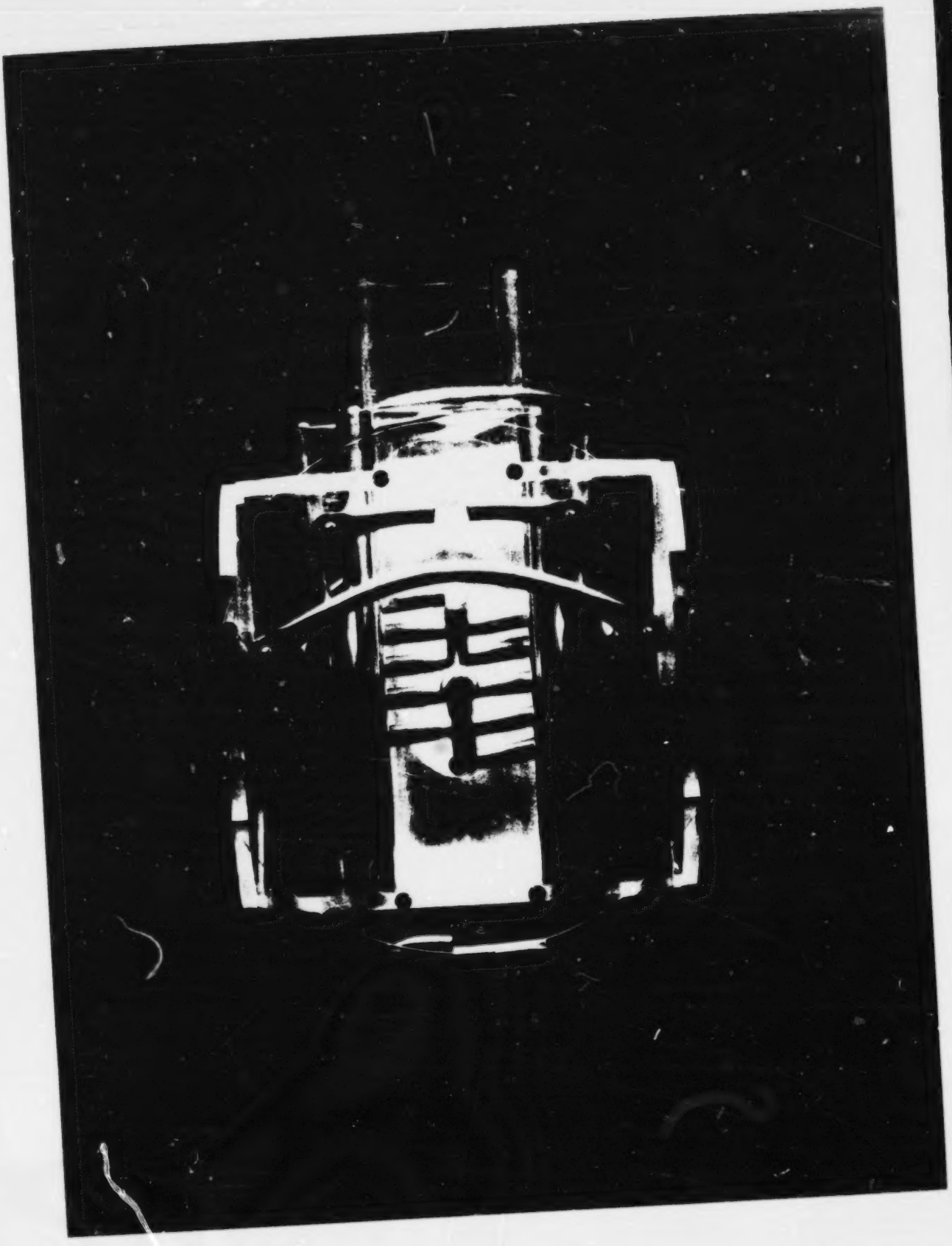

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Biomedical Engineering and Instrumentation Branch

Murray Eden, Ph.D., Chief

Opportunities for technology to play a role in making NIH more efficient presented themselves during the year—among them a better way to assure the safety of some 2,000 instruments used in the Clinical Center.

The problem: five separate tests were being performed sequentially on each instrument, the results recorded manually, and then transcribed into a computerized recordkeeping system—altogether an extremely time-consuming procedure. The solution: BEIB has reduced the work time dramatically with the creation of a custom electrical safety checker.

Each Clinical Center instrument now bears a bar coded identification label which can be read by the safety checker. This is recorded on a tape cassette. The safety checker then sequences through the tests. Results also are recorded on the tape so they can be automatically analyzed and documented by the computer to determine whether the instrument meets safety specifications. The checker makes it possible to accomplish in days what formerly took weeks for the periodic tests of all the instruments.

During the year, the Branch pursued its main mission of providing a wide variety of specialized engineering and physical science skills to the NIH research community. BEIB engineers collaborated in more than 200 projects to produce advanced instrumentation models, methods, and techniques dedicated to the acquisition of biomedical information previously not available to the research scientists.

The staff of 35 professional physical scientists and engineers and 75 technical support personnel responded to over 3,000 requests for the fabrication and modification of laboratory devices and made another 8,000 repairs or minor changes to scientific equipment.

New Imaging Systems

One area of technology which has grown in importance in both basic biological and clinical research is imaging. In prior years, the Branch has made contributions to ultrasound by developing a real-time sector scanner for cardiac visualization. In FY 1981, the Branch completed construction of two major new instruments, an NMR imaging system and a positron emission tomographic scanner (NEURO-PET). The latter is an example of the collaborative approach to NIH projects. Conceived by scientists at the National Institute of Neurological and Communicative Disorders and Stroke, BEIB designed NEURO-PET's mechanical and electronic parts, while a novel ring of scintillation crystals and the high speed electronic circuits were fabricated under contract with industry.

The NMR imaging system undertaken with support from the National Institute of Child Health and Human Development is based on a revolutionary method of generating images rapidly, rotating frame zeugmatography. Because NMR imaging does not use ionizing radiation, it is particularly promising for diagnostic studies on neonates. An imaging facility designed to provide elemental maps of biological objects viewed at the electron microscope level was developed in collaboration with specialists from the Division of Computer Research and Technology. All three systems currently are being tested and should be on line in FY 1982 for common use by NIH scientists.

BEIB's professional staff functions under four sections and a program in physical microanalysis which is contained within the Office of the Chief. Here is a brief review of FY 1981 activities:

Applied Clinical Engineering Section

This multi-disciplinary group, physically located in the NIH Clinical Center, integrates engineering concepts with biomedical research. Among other projects, the Section has joined with the National Cancer Institute's Clinical Pharmacology Branch in investigating cancer cell kinetics, concentrating on clinical chemotherapeutic treatment schedules. A multiparameter, triple laser flow cytometer is under development that will exploit immuno-fluorescent tagging techniques necessary for the analytical separation of clinical cell samples into various subpopulations. This will enable the various cell types to be studied for their pharmacologic responses.

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Engineering expertise is being melded with National Institute of Allergy and Infectious Diseases' research interests to expand the capabilities of another flow cytometer employed to answer basic biologic questions about an incurable and often fatal parasitosis known as Chagas disease. The device is used to perform cytometric analysis of DNA content on the causative agent of the disease, an obligate intracellular protozoan parasite known as *Trypanosoma cruzi*. The project is seeking to understand how the disease presents itself in nature in order to prevent the infection process.

The Section also embarked on a new area of research interest concerning core body temperature regulation. By incorporating computer-based instrumentation, the body's thermoregulatory system can be synthesized and the body's core temperature can be sustained at above or below normal for 24 hours or longer. It is to be hoped that information can be extracted which will reveal the hormones' role in maintaining normal body temperature. Similar innovative instrumentation is being incorporated to permit investigation of another parameter affecting sleep, namely core body temperature.

Chemical Engineering Section

Section activities ranged from theoretical description of fundamental pharmacologic processes to the development of sophisticated instrumentation for the observation of biological phenomena.

We have continued to provide pharmacokinetic support to clinical trials of intraperitoneal chemotherapy for localized diseases. In one study, blood sampling catheters were placed in a peripheral vein, hepatic vein, portal vein, and peripheral artery. Timed measurements of drug concentration from these sites provided a unique opportunity for detailed pharmacokinetic analysis of hepatic and peritoneal events.

In animal studies, principals of chemical reaction engineering have been further validated regarding the proper incorporation of *in vitro* drug metabolism data into *in vivo* models. A theoretical analysis of the role of the lung in pharmacokinetics has been completed. This work was stimulated by several recent collaborations involving drugs exhibiting very high rates of elimination from the body. The Section's interests in pharmacokinetics and synthetic membrane technology also are merging in the development of a system for continuous blood plasma sampling during a pharmacokinetic experiment.

Innovative application of materials has yielded considerable progress toward the development of a new artificial heart valve and a microcatheter for interventional radiology. Similar to the natural aortic valve in design, the artificial valve is injection molded in a unique manner to produce the necessary rigid and flexible areas by selective use of different molecular weight polymers. The microcatheter is an advance in miniaturization and consists of an integral balloon design with a calibrated perfusion port.

Work on tiny fiber-optic chemical sensors for physiological use is being continued with the development of an oxygen sensor. It is based on the old but little used principle of the quenching of dye luminescence by oxygen. The sensor offers the possibility of a significant improvement in instrumentation for measurement of oxygen in blood and tissue.

The Section also is working on advanced methods for ascertaining amino acid sequences of proteins to determine their biological functions.

Electrical and Electronic Engineering Section

The Section continued development of new applications for microprocessor-based "smart" instruments and IEEE-488 bus oriented instrumentation systems. Work in these areas is exemplified by a second generation automated test set for checking electrical safety of apparatus used in patient care, and a large and versatile fermentation system.

The main area of increased emphasis, although not new, is electro-optics. The addition of a staff member with special knowledge in this field, collaborating with existing experts in biophysics and electronics, has produced a team capable of attacking more difficult and diverse projects at a higher level of sophistication than heretofore.

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Examples of new projects include measurement of laser-induced absorption anistropy of biomolecules, optical measurement of platelet condition, computer controlled visual stimulation for evoked response studies, and enhancement of vidicon linearity in pico-second spectroscopy.

Conventional electronic instrumentation received substantial effort, the largest single project being the NEURO-PET scanner which is approaching completion. Work is also continuing on the NMR imaging system.

Mechanical Engineering Section

A number of analytical and experimental projects were initiated over the past year which include studies of cryogenic organ preservation, osmotic effects in tissue transport, mechanics of red cell membranes, and studies of the mechanics of muscle sarcomeres. A theoretical continuum model of the left ventricle is being developed to aid in the understanding of myocardial blood flow and muscle contractility. Particular attention is given to anisotropic effects due to the fiber architecture. Also an effort is being made to extend the current theory of muscle contraction to the three dimensional geometry of the heart wall. A model such as this will help to interpret data from dog experiments and suggest the course of future experiments.

During the past year a large quantity of experimental data on the transport properties of tumors has been collected using *in vivo* fiber optic microfluorimetry system developed by members of the Section.

A miniature microtome that can fit within the chamber of a scanning electron microscope has been constructed. This device will make it possible to obtain a large number of serial images of successive cross-sections of embedded biological tissue. Sections 0.5 micron thick have been cut, and work is progressing on finding embedding media to increase resolution. The microtome is adapted to the microprobe of the BEIB Analytical Methods Group, and the images can be handled by their computer to produce three-dimensional reconstructions of the tissue.

A microcalorimeter with a baseline stability of less than 1/5 microwatt was developed with the aid of lumped parameter modeling techniques. The instrument can detect as little as 10_9 moles of reagent and will be particularly useful for determining enzyme-substrate heats of reaction and the efficacy of various chemotherapy agents on cancerous cell metabolism.

Analytical Methods Group

The staff continues its work in three areas of research: elemental microanalysis, mass spectrometry and analytical ultracentrifugation.

In the first of these, procedures are being developed to address the special problems posed in microanalysis of biological materials using analytical electron microscopy. Quantitative analysis of the elements of interest in volumes of biological fluids of the order of 10^{-10} liter (microdroplets) is possible using x-ray microanalysis in the electron microprobe. Interfacing of a large laboratory computer to the 200 keV electron microscope is in an advanced stage to permit high speed transfer of images and spectra. This will allow the investigator to effect data reduction and manipulation of both spectra and images and then utilize the results to determine the next step of the analysis.

In the second area, a system, designated Secondary Emission Mass Spectrometer (SEMS) is being developed to study secondary emission processes on surfaces under bombardment by electrons, ions, and neutral particles in connection with ionization of organic materials. It also makes it possible to detect sputtered secondary ions and transmitted ions (positive and negative), to detect optical emission of sputtered particles, and to store certain ions for certain periods of time in order to obtain higher sensitivity and selectivity of the mass spectrometric analysis.

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In the third area, a laboratory minicomputer has been interfaced to the microcomparator used for measurement of photographic records from the analytical ultracentrifuge. In addition to permitting the more rapid and accurate acquisition of much larger quantitites of data, this system permits preliminary data processing and editing and then transmittal to the DEC-10 computer for analysis through the use of mathematical models. Significant progress has been made toward interfacing this computer directly to the UV absorption scanning system of the analytical ultracentrifuge.

Scientific Equipment Services

This group continued to provide scientific equipment design, fabrication, repair and rental services to the NIH scientific community. The workload has remained constant at about 11,500 work requests costing about $4 million.

Measures are being taken to increase operational efficiency by decreasing response time to service requests and reducing the cost of the services. These initiatives range from changes in work processing procedures to the use of automated fabrication equipment.

Rental Program

Use of the scientific rental program by the NIH community increased during the year. The number of pieces of equipment available for rent rose from 1,375 to 1,820 with a value of $4.4 million. At year's end, nearly 80 percent of the inventory was in use, indicating widespread acceptance of the program's cost saving benefits.

Outlook for FY 1982

The opening of the Ambulatory Care Research Facility (ACRF) will place an additional workload on BEIB. In anticipation of this increase, BEIB is initiating a contract for the electrical safety testing and preventive maintenance of equipment in the Clinical Center and the ACRF.

Anticipated activities of the Electrical and Electronic Engineering Section include completion of major projects; consolidation and extension of recent new initiatives in the areas of micro-processors, bus-oriented systems, and electro-optics. The NEURO-PET, for example, will require a great deal of further effort for testing, evaluation, extension from 1 slice to 7 slice imaging capability, and development of hardware and software techniques for suppressing scatter artifact. In the area of micro-processors, we will be establishing a second system to support developmental work.

In the Applied Clinical Engineering Section stress will be placed on continuing both instrumentation and modeling in flow cytometry and in developing a new area of investigation that deals with coronary resistance as well as the relation of coronary flow to left ventricular wall dynamics as observed by echocardiography.

In elemental microanalysis we expect to record electron energy loss spectra from a series of fluorinated biological molecules. We also will be studying radiation damage effects to various types of samples.

In the area of analytical ultracentrifugation we expect to develop improvements in the data acquisition system and to increase the precision of the scanner system using photon counting. Work will continue on measurements of thermodynamic parameters of biological macromolecule self-association and ligard binding.

Anticipated new projects for the Mechanical Engineering Section include: a monolithic silicon-A1 thermopile (collaborative project with Electrical Engineering Section); ultrasonic measurement of arterial plaque thickness; and a new type of electromagnetic blood flowmeter which utilizes simpler probe design.

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The Chemical Engineering Section is expected to place increased emphasis on environmental contaminants with consideration of the role of pharmacokinetics in supporting risk estimates in man. The development of mathematical models for the refinement and improvement of bioassay techniques will be continued.

Work on the application of synthetic membranes in biomedical research is expected to lead to preparation of a proposal to the North Atlantic Treaty Organization for sponsorship of a two-year NATO Advanced Study Institute. The Institute will provide young investigators with an intensive introduction to synthetic membrane science and applications. In cooperation with the Office of Medical Applications of Research, the section will organize a Consensus Development Meeting on "Clinical Applications of Biomaterials." The meeting will examine critical technological, ethical, legal and financial issues concerning biomaterials in the practice of medicine.

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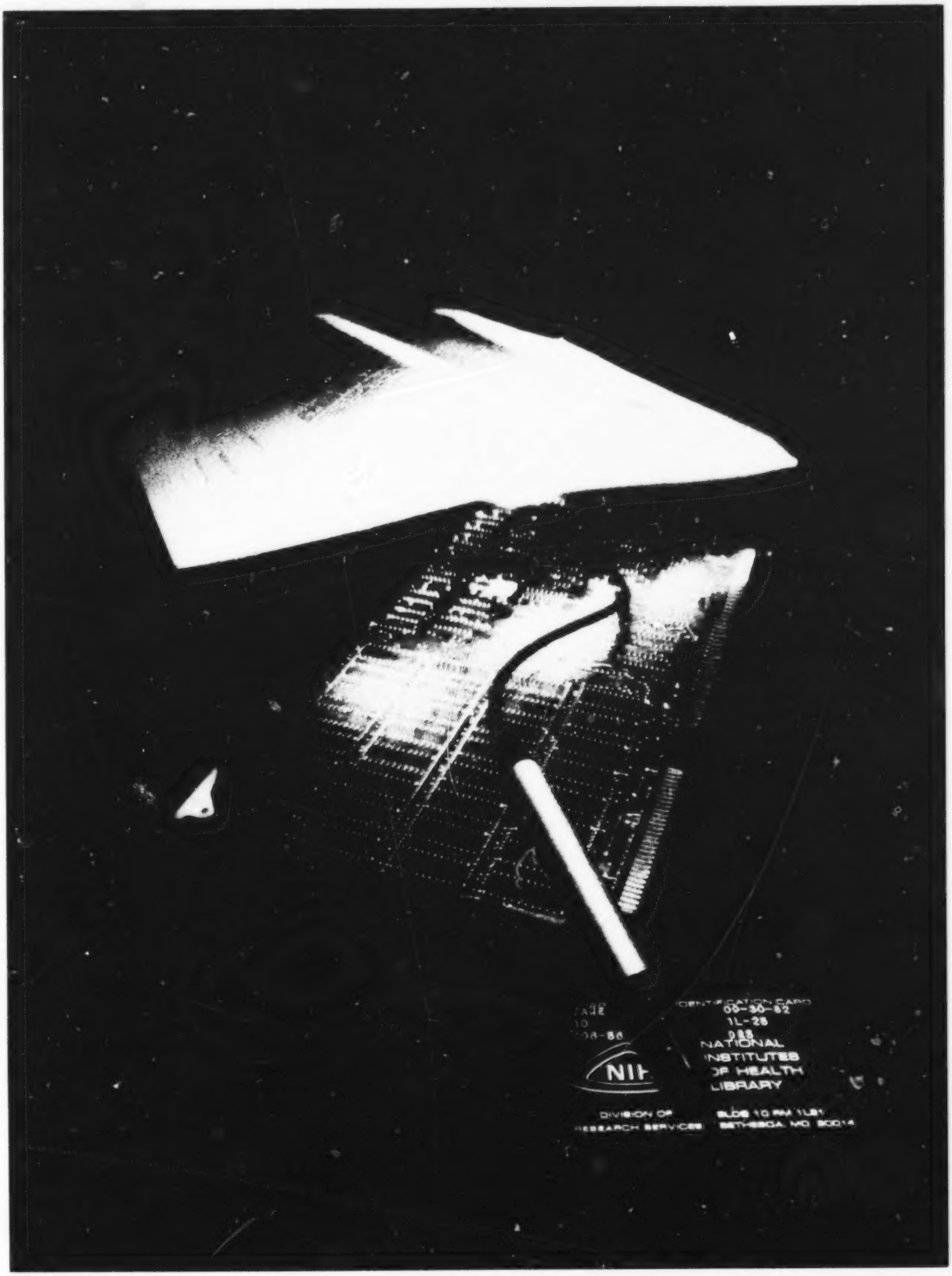

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Library Branch

John Smart, Acting Chief

More progress was recorded during the year in the NIH Library's continuing efforts to improve the quality of its services and to increase efficiency through automation. Here are the highlights of FY 1981 activities:

Reference and Bibliographic Services Section

Computerized bibliographic searches continued to be the fastest growing service of the Library. More than 35,000 searches were performed, a 15 percent increase over the previous fiscal year. Improving further on the range and depth of data bases, the System Development Corporation was added to the list of vendors that already included the National Library of Medicine, Lockheed, and Bibliographic Retrieval Services.

An important feature of the bibliographic search service is the Selective Dissemination of Information (SDI) program, which provides biweekly and monthly current awareness searches for NIH personnel in subject areas of continuing interest. There were over 300 SDI search profiles this year.

The Library's public relations program was broadened. Brochures were issued giving a general view of the Library and its services and the computerized search service. A series of seminars and lectures were conducted on search services and specific data bases.

To enhance efficient utilization of the Library's limited space, a review was conducted during the year of 900 ceased and discontinued journal titles to determine ones that could be removed from the shelves. Experts from the NIH community are advising the Library in the drafting of a comprehensive retention policy covering the approximately 6,000 journal titles in the collection.

Technical Services Section

The Monographs Processing Unit began implementation of the Anglo-American Cataloging Rules, second edition (AACR II), as interpreted by the Library of Congress, along with newly published revisions of the OCLC (Online Computer Library Center, Inc.) cataloging manuals. This is to ensure that the Library's cataloging practices meet both national and OCLC standards.

The Library's budget for monographic acquisitions remained unchanged from the previous two years despite the rising cost of technical materials. Accordingly, some purchases have been deferred.

Readers Services Section

Selected non-print items devoted to clinical education were transferred to Clinical Center departments where it is expected they will find greater usage.

Outlook for FY 1982

The Library is on the way to becoming fully automated. A computer-based system—already in place for bibliographic searches and circulation control—is in the process of being extended to acquisitions, journal control, and other services.

When completed the data base will reflect the Library's total holdings. The staff will be able to monitor and analyze the collection, observing acquisition patterns and usage trends so that services may be improved. The circulation control system will increase operational efficiency in the charging and discharging of books, renewing charges, reserving materials, and other activities.

In addition to moving toward full automation, the Library will continue reviewing the journal collection and replace some titles by microfilm in order to accommodate shelf space limitations.

As a faster means of disseminating information on newly acquired titles, the Library will make the data available on WYLBUR, at the central computer system maintained by the Division of Computer Research and Technology. The file will be updated weekly. Printed copies of the list will be distributed to those without access to WYLBUR.

Services of the NIH Library

The NIH Library offers a full array of services to assist scientific investigators in their work. They include:

- **Bibliographic Services** - A staff of six specialists perform literature searches and compile bibliographies upon request. The staff is experienced in retrieving citations and abstracts from some 155 data bases to meet investigators information needs and keep them informed through monthly updates of new literature published in their fields.
- **Reference Services** - The Library fulfills requests for literature references by telephone as well as on site.
- **Photocopying Services** - High speed photocopying machines are available to users. The Library also fullfills copying requests.
- **Reader Services** - Library users may be placed on circulation lists for newly received journals. Research works not in the collection are available through interlibrary loan. There is a translation service for foreign language materials.

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Medical Arts and Photography Branch

Arthur F. Moore, Chief

Demand for graphic arts services increased again in FY 1981, continuing to reflect the expanding amount of new biomedical knowledge being generated by NIH investigators. Most of the Branch's work assists scientists in recording the results of their research and communicating it in seminar presentations, published articles and papers.

The Branch's staff of 49 artists, photographers, and other specialists are highly skilled in meeting the needs of scientists for graphic presentations, still and motion picture photography, including photomacrography and photomicrography, and medical arts. Services also include the design and production of publications; the preparation of slides, vugraphs, and other projected visual aids; animation artwork; technical, general, and medical illustrations; exhibit design; statistical drafting; display charts; posters and medical models.

The philosophy of the Branch is to provide high quality professional services competitive in cost with commercially obtainable services. The staff monitors all graphic and photographic services procured from outside vendors to assure quality standards are kept.

The heavier demand for finished artwork during the year was met by a corresponding increase in contract services and an acceleration in deliveries. Photographic services and graphic services were performed normally in five work days, with 24-hour emergency service available when necessary. Design work was turned out in 10 workdays.

The Branch has extensive expertise in conversion of data into effective multimedia presentations. This counsel is readily available for all of the Branch's services and should be used earlier and with more frequency.

A graphic design manual prepared by the Branch is available to investigators to assist them in planning and producing desired visual communications. This publication is gaining wider acceptance and is helping to effect savings by establishing standards and reducing preliminary design problems. Following is a summary of FY 1981 activities:

Photography Section

Technological improvements were instituted in the areas of photomicrography, photomacrography, and photographic laboratory services. They were accomplished by increased technical training of personnel and by replacing old equipment with advanced photographic tools. The section employed outside vendor services from private photo firms in the Washington, D.C. area in addition to in-house facilities, in order to keep pace with the calls for photography services.

Design/Graphics Section

This unit is composed of highly trained, extremely dedicated personnel. The group is capable of filling requests for complex visual productions, which are continually mounting in number. The section had a productive year, augmenting output with no increase in personnel and maintaining its usual high quality production.

Medical Illustration Section

Requests for medical illustrations remained at a normal level throughout the year. Contracting was seldom used since few projects entailed short deadlines. Calls for medical models remained about the same as in FY 1980.

Motion Picture Section

The number of filming requests were about the same as 1980 with several more formal productions completed than in the previous year.

Outlook for FY 1982

The Branch is planning an educational campaign within the NIH community to inform scientific investigators how they can reduce the ever-mounting cost of graphic arts services. First among these is to use the 24-hour rush service, which costs 50 to 100 percent more than regular service, only when absolutely essential.

Guidelines to be published in articles and notices will stress the benefits that can be derived from investigators thinking through how they want their articles and presentations illustrated and adhering to the plan once it has been firmed up with MAPB. They will be advised to submit complete, clear, and accurate raw data for display. These procedures will avoid the need for rush service to meet deadlines. They also will eliminate the need to make changes in artwork after it has been prepared. Such changes or corrections can double the cost of the original work.

Investigators will be asked to order only those copies of slides and pictures which are necessary, eliminating "just in case" extras to save costs. Moreover, they will be told how to protect artwork for future reprinting. Replacement of damaged materials can be as costly as the original.

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Veterinary Resources Branch

Robert A. Whitney, D.V.M., Chief

In its role of providing animals, research support, and veterinary services to the NIH intramural program, the Veterinary Resources Branch has become a focal point for monitoring national and international developments which may affect the utilization of animals in biomedical research. Among the concerns are issues surrounding the use and care of animals in research.

During the year, the Branch found itself serving increasingly as an information source for the national news media. As public interest heightened in animal care issues, newspaper, magazine, and radio and television reporters turned to the Branch frequently—and sometimes daily—for interviews and data on various subjects. The Branch was able to meet these requests using information based upon reporting required of NIH by the Animal Welfare Act and the staff's extensive knowledge of the field.

Another example of the Branch's widening responsibilities is the Interagency Primate Steering Committee (IPSC), which is administered by VRB. During the year, the IPSC continued to work with the World Health Organization in developing a contract to ensure the availability of primates for human health research. The contract will assist Asian and African nations in conserving and breeding indigenous primates and is similar to activities being carried out in Latin America under contract with the Pan American Health Organization.

The VRB assisted in establishing an Image Analysis Center for Ecological Studies through the Smithsonian Institution. The center will use imagery obtained from satellites to evaluate the quantity and quality of habitat available to primate species and recommend actions to prevent deterioration as part of the overall conservation effort.

Following are summaries of VRB activities during FY 1981:

Comparative Reproduction

The Branch's principal interest in comparative reproduction is to provide cryopreservation of embryos. The program is designed to preserve valuable inbred species of VRB's Genetic Resource for future NIH research needs and to reduce genetic drift in breeding colonies (see accompanying article on page 19). Another advantage of this program is a capability of rapidly establishing a rodent strain threatened by loss through disease.

A separate cryopreservation activity involves the collection and storage of semen obtained from animal species important to the study of specific human disease problems. Normal semen also is stored and used to improve the reproductive efficiency of research colonies of dogs, swine, and sheep.

VRB is collaborating with NIH institutes and other Government agencies in studies to better understand and improve reproduction in laboratory animals. Examples of these projects include: artificial breeding and preservation of semen from dogs with hereditary subaortic stenosis for the National Heart, Lung, and Blood Institute; fertility evaluations of inbred miniature boars used by the National Cancer Institute; collection and preservation of gametes, characterization of the reproductive cycles, and artificial insemination of primates. The results of studies conducted in the VRB canine, nonhuman primate, and livestock colonies also have been applied to enhance reproduction in these animals.

Animal Center Section

This Section produces, maintains, and develops large laboratory species—chiefly farm animals, dogs, cats, and primates—and provides related services and products for NIH investigators. Genetically defined foxhounds, swine, and monkeys are provided by breeding colonies, and various other animals are purchased, quarantined, and conditioned for research.

Cynomolgus monkeys from Philippine and Indonesian sources are being quarantined because of the continued unavailability of imported rhesus monkeys. Bans on the shipment of rhesus monkeys by major source countries have virtually shut down the supply of these animals since January 1979. Overall, research requirements for nonhuman primates have increased; cynomolgus and squirrel monkeys are being substituted for rhesus monkeys in some studies.

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VRB contract production colonies of rhesus monkeys are being expanded to supply intramural programs and other Government agencies, in accordance with National Primate Plan objectives (Figure 1). Male rhesus monkeys produced by these colonies are being utilized for polio vaccine testing, and females are being held as replacement breeders. Cynomolgus and a variety of New World monkeys are being incorporated in the breeding program. Under an interagency agreement, breeding colonies of two species of tamarins (*Saguinus labiatus* and *S. mystax*) were established at the Animal Center for hepatitis research by the Food and Drug Administration's Bureau of Biologics.

Requirements for dogs, cats, and canine blood decreased during the year because of changes in intramural research programs. Adjustments were made in the canine breeding colony to produce 600 dogs per year. The number of cats procured, quarantined, and issued is expected to stabilize at 600.

Comparative Pathology Section

This section is responsible for defining the health status of laboratory animals produced, quarantined, or used in research at the NIH. It also assures the genetic quality of NIH animals shipped to laboratories throughout the world as a function of the Genetic Resource.

The number of autopsies performed by the pathology service was 4,095. This is approximately 13 percent less than last year (Figure 2) when the number was unusually high as a result of an outbreak of mousepox at NIH. The number for 1981 remained relatively high, due in part to an outbreak of mouse hepatitis in the VRB barrier-maintained colonies. Many autopsies were done through the Animal Disease Investigation Service (ADIS) on animals maintained by NIH investigators. Often infectious disease problems occur as a result of pooling animals from diverse sources; much of the work of the ADIS is done to delineate naturally-occurring disease from experimentally induced conditions.

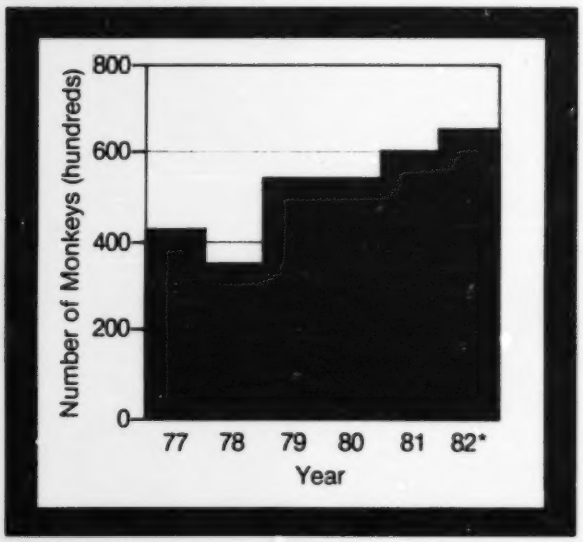
Two major investigations were conducted of genetic contamination in inbred BALB/c mice produced for NCI under contract. The results indicated contamination by an outbred strain of Swiss-Webster origin. Two histocompatibility haplotypes and five enzymes were found in the contract mice that are not normally carried by BALB/c mice.

New computer systems were designed and programmed for data analysis that permit the differentiation of strains of mice and rats by both their genotype and phenotype. All animal breeding records, immunological and biochemical data, and the freezer catalogue for tissue samples are now maintained by the laboratory's computer system.

Small Animal Section

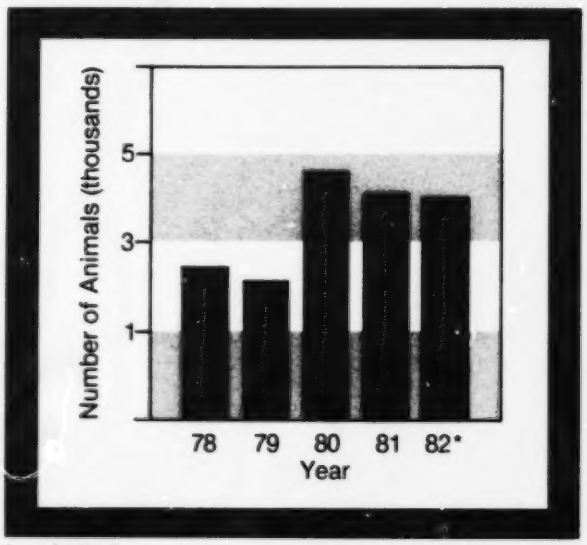
Approximately 950,000 rodents and rabbits were issued for intramural research—a slight decrease from last year (Figure 3). Utilization of all species produced by VRB decreased, while use of guinea pigs and rats from contract sources increased

Figure 1
Rhesus Monkey Production for NIH Intramural Programs



*projected

Figure 2
Animals Autopsied



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slightly. Production colonies of Strain 2, Strain 13, and NIH guinea pigs were contracted to commercial breeders; foundation and pedigree expansion colonies will remain at NIH. Genetic integrity of the VRB colonies remained uncompromised, and the composition of the Genetic Resource was stable. However, the appearance of mouse hepatitis virus (MHV) infection in the barrier facility resulted in the loss of several new nude mouse congenics. Until the mouse foundation colonies within the barrier are rederived to eliminate MHV, development of new mouse congenics and the introduction of new strains and stocks will not be undertaken.

Development of new rat models continues since this species is not affected by MHV. The N:NIH outbred rat was developed for use on general population studies, and the toothless (*tl*) and osteopetrotic (*op*) genes which produce alterations in the immune system, as well as skeletal defects, are being established in inbred rats. Similarly, the corpulent (*cp*) and diabetes insipidus (*di*) genes were established in two inbred strains. The outbred Wistar-BB rat, characterized by juvenile onset diabetes, was introduced into the barrier. A production colony of nude (*rnu*) rats also was established.

Chemical contaminants in laboratory animal diets continue to be a concern to NIH investigators. Preliminary study results indicate that every production batch of natural ingredient diets contains traces of heavy metals, but at concentrations below those shown to adversely affect diet quality. A majority of the feed samples analyzed also contained at least some chlorinated hydrocarbons and organophosphates, but the concentrations were lower than those in commercially available certified diets. There are occasional samples that contain levels of a single contaminant that may be cause for concern, but it has not been possible to verify whether these high concentrations are real or due to analytical or sampling errors. Random analyses for nitrosamines indicate that their concentrations are considerably below the levels that have been reported to adversely affect experimental results. However, in view of the investigator concerns, efforts are being made to develop new rodent diets formulated with ingredients that have a low potential for these contaminants.

Veterinary Medicine and Surgery Section

Renovations to the central animal radiological and surgical facility were completed. This area can accommodate a wide variety of animals ranging from mice, dogs, and nonhuman primates to small livestock such as sheep, goats, and swine. Staff veterinarians provide complete services in accordance with research protocols and assist in developing new animal models.

The primate recycle program continued to issue animals at a high rate as a result of the unavailability of rhesus monkeys from regions with indigenous populations (Figure 4). Issues of neonates from timed pregnant primates were adequate to meet anticipated needs. Although the use of dogs declined, the trend towards increased utilization of sheep and goats continued.

Figure 3
Small Animals Issued

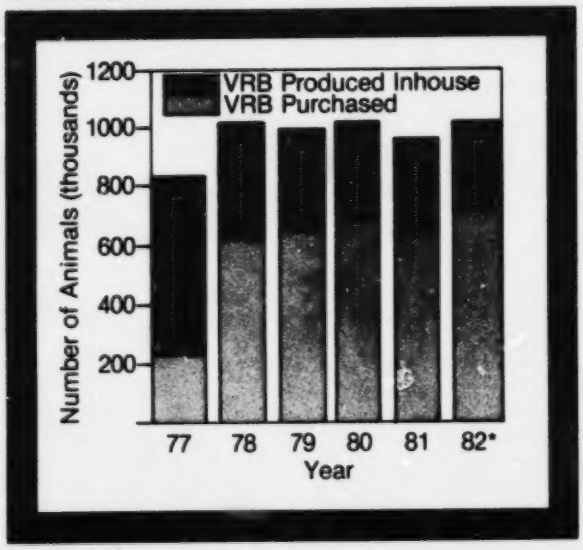

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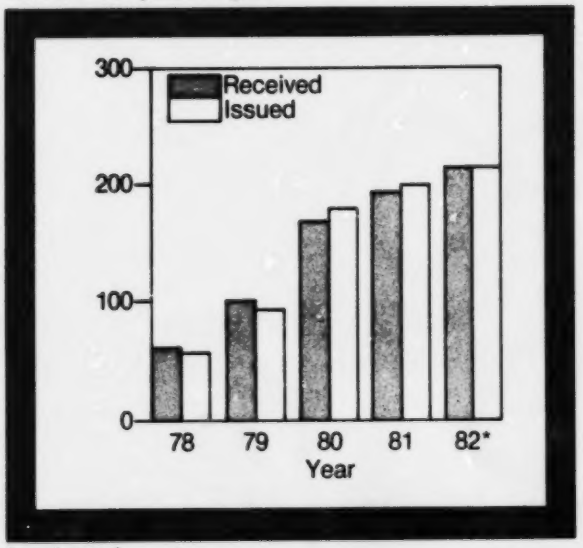
Figure 4
Primate Recycle Program



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Outlook for FY 1982

The Animal Center will begin to produce beagles for NCI programs in space that is becoming available as a result of decreased demands for foxhounds. Facilities for livestock will be developed. Breeding contracts for rhesus and cynomolgus monkeys will be expanded to better accommodate the needs of the research community for these species. In-house, VRB primate programs will become more involved with the breeding of New World primates and research holding activities. The data processing system developed for the Carnivore Unit is being expanded to encompass other activities at the Animal Center.

Renovations in the Small Animal Section will provide a central research rodent holding facility for NIH investigators. A contract to design a data processing program will be awarded in FY 1982. When fully implemented, the program will permit the section to be more responsive to NIH research needs in terms of colony maintenance, issues, and billing procedures.

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VRB's Genetic Resource—a Unique Service to the Biomedical Community

Stephen Potkay, D.V.M., Deputy Chief,
Veterinary Resources Branch

Early in the 1960s researchers at Japan's Kyoto School of Medicine came upon a male rat afflicted with naturally occurring hypertension. Through a series of matings and inbreeding, they developed a colony of hypertensive rats with one subgroup possessing extremely elevated blood pressures—a condition that made them excellent models for the study and treatment of this illness in man.

Today, descendants of the original Kyoto colony live on at the Veterinary Resources Branch. Known as SHR/N (spontaneously hypertensive rat) the descendant colony, including sublines, is part of the VRB's Genetic Resource, a repository of more than 200 genetically defined strain stocks and mutants of mice, rats, and other small research animals maintained as a unique service to the biomedical community in the U.S. and abroad.

Catalogue of Available Animals

The composition of the resource is continually changing either through the introduction of new genetically defined animal models obtained from institutions around the world or through the development at VRB of new models employing internal strains and stocks. VRB seeks to preserve strains, within the limits of its capabilities, that are able to meet the present and future needs of a broad spectrum of research.

There are eight species of rodents and rabbits characterized as either outbred stocks which are maintained by random mating or as inbred strains produced by brother-sister matings. Congenics, which are genetically identical to an established inbred strain except for a short chromosomal segment bearing a "foreign" gene, also are maintained along with recombinant inbreds which are developed by the brother-sister matings of the progeny from the cross of two inbred strains.

A full listing of the strains available in the resource may be found in the recently issued *NIH Rodents 1980 Catalogue* (NIH Publication No. 81-606) which may be obtained by writing the Veterinary Resources Branch.

Responding to Changing Needs

The Veterinary Resources Branch was created in 1948 as the Laboratory Aids Branch to support NIH intramural programs by providing healthy research animals and animal care related services. During the ensuing years, research investigators have focused increasingly upon more precisely defined animal models for studying human illness such as hypertension, diabetes, dwarfism, arthritis, glaucoma, retinal dystrophy, autoimmune hemolytic anemia, and a host of parasitic and infectious diseases. Requirements also have become more defined in terms of animals used for vaccine testing, carcinogenesis, immunologic studies, and other basic research. The result has been a change in direction for many VRB programs, from large-scale production of outbred (heterogenic) stocks to the production of numerous and diversified, congenic recombinant inbred strains of rodents. Within recent years, these efforts have also extended to the development and production of genetically defined swine, sheep, and dogs.

The development, production, and maintenance of defined animals would not be possible without appropriate management strategies for genetic and health quality control. Assurance of genetic integrity is based first on carefully conceived methods of handling, breeding, and housing animals that are followed in all the colonies in a manner that is practically ritualized. Animals produced are subjected to genetic monitoring utilizing profiles of morphologic, biochemical, and immunologic markers which, like fingerprints, identify specific strains of mice, rats, and guinea pigs.

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Protecting the Genetic Resource

A variety of microbiological techniques are similarly applied to monitor the health status of animals maintained in and produced by the Genetic Resource. The techniques vary according to the conditions under which animals are housed. These include germfree, gnotobiotic, barrier maintained, and conventional environments.

Although health monitoring is intensive and involves a full spectrum of pathology and microbiology services, it serves principally to define animals with regard to their association with parasites such as bacteria, viruses, protozoa, helminths, etc. Maintaining animals free of such organisms is accomplished by preventing their entry into the colonies. There are rigid procedures for personnel who care for them, and for keeping facilities in a clean and sanitary fashion.

In this regard, the adaptation of germfree and barrier room technology to the Genetic Resource activities has been effective in reducing the risk of catastrophic loss of irreplaceable genetic material through disease outbreaks. These techniques have been indispensible for protecting and maintaining animals with profound immunological defects, thus extending the variety of animal models available for research.

Embryo Cryopreservation

Recently, VRB initiated a cryopreservation program of mice embryos to enhance the protection, efficiency, and utility of the Genetic Resource. Techniques have been tested to collect genetically defined embryos from females shortly after conception and preserve them in liquid nitrogen for later reimplantation in surrogate mothers. The tests show frozen embryos may be held indefinitely and still remain viable at the time of reimplantation.

When fully developed, the program is expected to bring considerable savings in labor and materials. This would come about by preserving entirely by embryo freezing valuable strains not currently in use, eliminating the cost of maintaining live stocks. Further savings may be obtained by serving research laboratories with frozen embryos instead of live animals. It is estimated that up to 60 percent of the strains in the Genetic Resource could go into the freezer with a 60 percent cost saving. This would also free up space for the raising of more difficult strains that are not being produced at present. One of the additional benefits in cryopreservation is that it prevents genetic drift which can occur in laboratory animal colonies maintained over a long period.

There is a nutrition program for the resource in which dietary requirements of the various species and strains are studied and new diets developed to meet specific needs. Particular attention is given to dietary quality control and analysis of feeds for selected potential contaminants.

During the fiscal year, breeding nuclei of various strains were shipped to a dozen countries, including the first shipment to the People's Republic of China. Approximately 3,000 breeders were made available to more than 60 institutions within the United States.

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